

A NON-HOMOGENEOUS BINOMIAL MODEL FOR THALAMIC OSCILLATIONS

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ABSTRACT- The thalamic ventral posterior lateral neurons (VPL) respond to somatosensory stimulation with a burst of action potentials followed by a periodic oscillation at the spindle frequency. This study aims to build a statistical model to quantify the multi-unit behavior and explain putative underlying mechanisms. Multi-unit data, comprising 4 or 5 different neurons, were collected from anesthetized adult rats ($n=2$) by positioning a microelectrode in the ventral posterior lateral (VPL) nuclei of the thalamus. Using an observation window of 1 ms and assuming that neuronal firing is uncorrelated within this window, the firing rate of the neurons can be successfully modeled by using a non-homogeneous binomial model with $N=1$ (with 99.5% confidence). Using maximum likelihood estimator (MLE) of the parameter p , statistically consistent prediction of the parameters of non-homogeneous binomial model was made using a minimum of 50 stimulus-response pairs. The inter-stimulus interval histograms of the individual neuronal firing indicate a possible stochastic resonance behavior that will model the spindles in thalamus. Our model offers a statistically elegant description of oscillations in neuronal action potential data and can in general, be used to track changes in the neuronal dynamics with function or dysfunction.

Keyword-Thalamus, oscillation, binomial model, spindle, stochastic resonance

I. INTRODUCTION

Neuronal oscillations have been observed in several regions of the brain either spontaneously or in response to periodic stimuli. However, quantification of these rhythmic oscillations has been confined to averaging histograms using auto-correlograms or post-stimulus histograms (for stimulus-response pairs) [1]. These histograms test for consistency in the observation but give no insights into the generating process, nor do they test for statistical significance. An earlier effort by Konig [2] attempts to fit a generalized Gabor function to histograms of periodic oscillations using least squares. The parameters of the Gabor function then quantify the oscillations. However, this model still does not describe the statistics of the generating process and may not be useful for mechanistic insights.

This study focuses on multi-unit oscillations observed due to a reciprocal interaction between reticular thalamic and dorsal thalamic nuclei in response to somatosensory stimulation [3]. Cortex-thalamus-cortex loops generate a powerful and coherent feedback onto the thalamus, resulting in highly coherent oscillations [4], and the

synchrony is also maintained by intrathalamic connectivity [5]. We investigate appropriate statistical models that can describe oscillations recorded from dorsal thalamic neurons and then attempt to make consistent estimates of the descriptors.

II. METHODOLOGY

Multi-unit data was collected from adult Wistar rats ($n=2$). Tungsten electrodes (FHC Inc., Bowdoinham, ME) were implanted in the thalamic ventral posterior lateral (VPL) area for recording multi-unit data. The rat was under barbiturate anesthesia (sodium pentobarbital) during the experiment. Periodic somatosensory stimulation was given every 3 sec. Data was acquired using Spike2 (Cambridge Electronic Devices, Cambridge, UK). The units were sorted using a template matching algorithm within Spike2.

Time-series analyses were performed on the successive spike-counts measured with bin width of 1 msec. The successive firing event of the neuron is not independent due to the modulation of the network of RT (reticular-thalamic) and VPL neurons, so the Poisson model is not suited here. But within a small time window of 1 msec, which is small enough for just one action potential, we fitted a non-homogeneous binomial model. A Maximum Likelihood Estimator (MLE) is used here to estimate the probability of the firing $P(t)$, which changes with time after the stimulus. Wilcoxon rank sum test is used to evaluate the statistical hypothesis. A p -value ($0 < p < 1$) much larger than zero indicates a good match between the model and the data. The evolution of estimated mean and variance of the firing probability was investigated every five stimulus to determine the minimum number of stimulus-response pairs needed to make a statistically consistent estimate of parameter $P(t)$.

Cross-correlation and power spectrum is used to investigate the relationship of $P(t)$ of two different neurons. To investigate the burst behavior in each spindle, we separate the 3 sec inter-stimulus interval into 30 segments and plot the ISI of each segment. The ISI plots were also examined for the presence of stochastic resonance.

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III. RESULTS

Thalamic oscillations have two components, a modulating spindle oscillation which is caused by cortex-

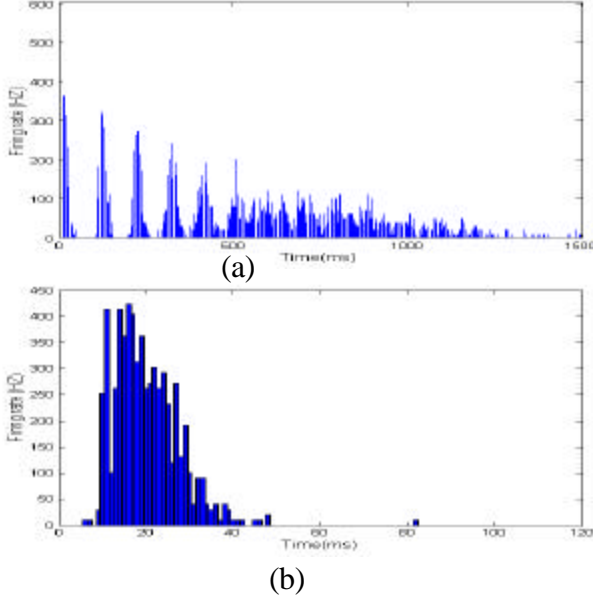


Fig. 1. Post-Stimulus Histogram (PSH) of (a). Thalamic oscillation (b). inner spindle burst

thalamus-cortex loops with frequency of about 10 Hz (Fig. 1(a)), and the inner spindle bursts (Fig. 1(b)).

Using one milli-second time bin with at most one spike (action potential) in each window, the whole oscillation can be modeled as a non-homogenous binomial process, where $P(t)$ (the probability of firing at time t) changes with time (Fig. 1(a)). The p -values from the Wilcoxon hypothesis tests at different times after stimulation are shown in Fig. 2. The large p -values during the times of

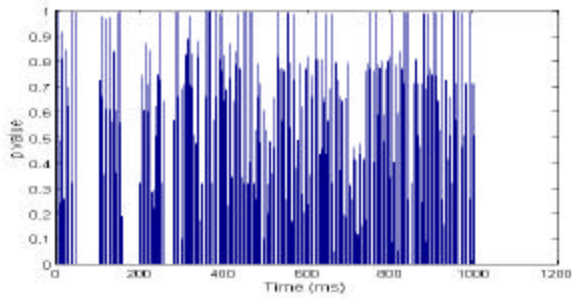


Fig. 2. Wilcoxon hypothesis test result

action potential firing indicate a good fit to the non-homogeneous binomial model.

Using a maximum likelihood estimator (MLE), we estimated the evolution of mean ($P(t)$) and variance of the firing rate at specific time-points after stimulus. The estimates are plotted against increasing numbers of stimulus-response pairs in Figs. 3(a) and (b). The two plots

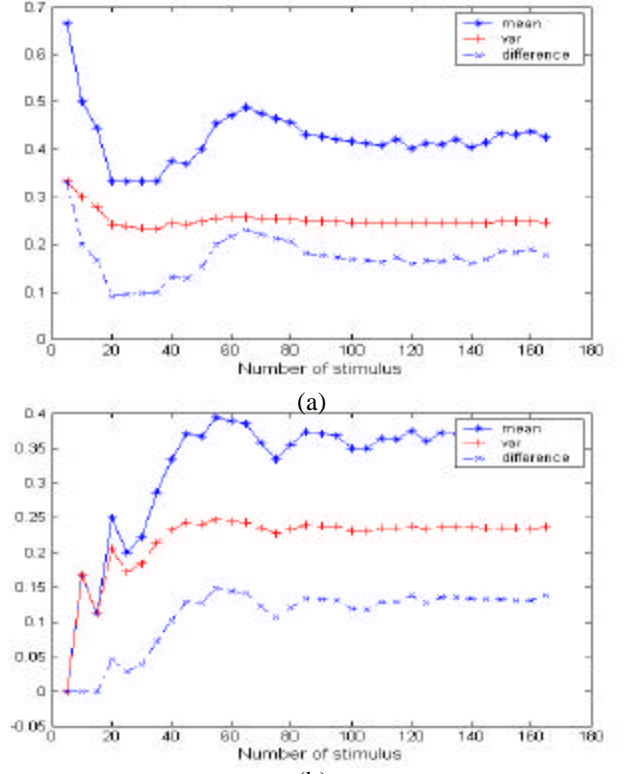


Fig. 3. Evolution of mean and variance at (a) the first peak ($n=16$ ms) and (b) the second peak ($n=122$ ms)

shown correspond to 16 msec and 122 msec after stimulus (corresponding to the first and second peak in Fig. 1(a)). Fig. 3 shows that the neuronal firing is a stationary random process. With approximately 50 stimulus-response pairs we can make a good prediction of the mean ($P(t)$).

After sorting the multi-unit data, we investigate the dynamics of each neuron. The power spectra of $P(t)$ of two neurons are shown in Fig. 4 with very similar profiles and fundamental frequencies. The cross correlation of $P(t)$ between the two neurons indicates a 1ms phase shift. Figs. 5(a) and 5(b) indicate that the most frequent occurrence of the inter-spike interval is around 3 msec for both neurons. There are also non-periodic fluctuations at 4ms, 5ms, and 6ms.

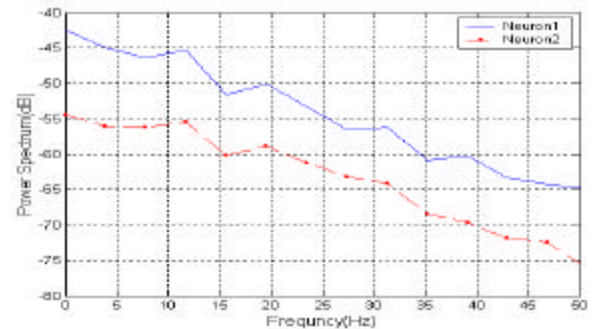


Fig. 4. Power spectrum of $P(t)$ of two neurons

IV. DISCUSSION AND CONCLUSIONS

A non-homogeneous binomial model has been used to describe the statistical behavior of the thalamic oscillations. Consistent estimates of the probability of firing, $P(t)$ can be obtained from a minimum of 50 stimulus-response pairs by using a maximum likelihood estimator (MLE). This provides an elegant statistical description of the thalamic response as whole and neuronal

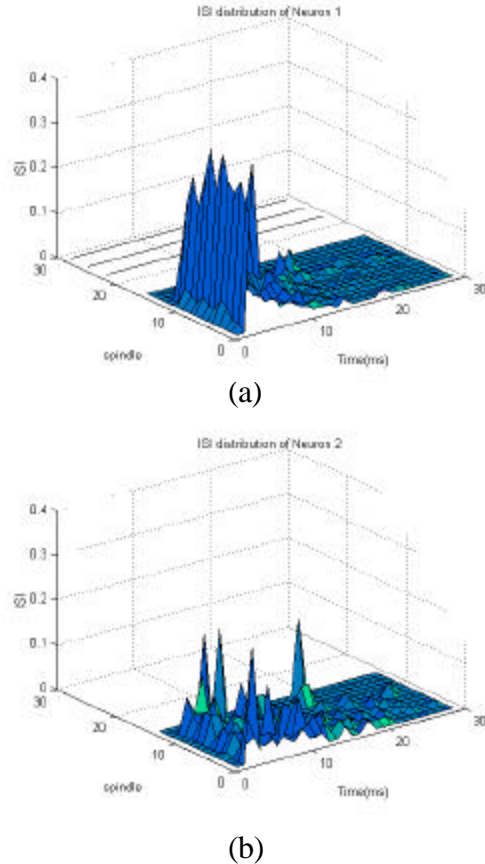


Figure 5: ISI distribution of each spindle after stimulation (a). neuron 1. (b) neuron 2. The spindle numbers correspond to the peaks in the histogram following the stimulus. Each peak corresponds to a spindle. The time labels corresponds to the time after stimulation.

oscillations in particular. Conventional methods to estimate periodicities in neuronal oscillations involve averaging of approximately 100 response histograms. The only known effort to quantify neuronal oscillations involves fitting a known periodic function to the averaged histogram [2], which does not describe the statistics of the generating process.

Results from cross-correlation indicate that the neurons fire synchronously with a constant time delay. In the ISI, there is a strong first peak at the time of about 3msec, which means the neuron most probably wait about 3msec

to fire again. It implies that in VPL there should exist an intrinsic periodic driving force, but it is not strong enough and must have the help of intrinsic noise to make the neuron fire [6]. In fact, Na^+ channels provide a possible source of intrinsic noise [7], and the network of oscillators may provide the intrinsic periodic driving force for each neuron [8]. Future work needs to be done by using stochastic resonance to understand the underlining mechanism of the non-homogenous binomial model.

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